

Set	Items	Description
S1	63402	MEASLES OR RUBEOLA
S2	23513	MUMPS
S3	3285	RUBEOLA
S4	4563637	CANCER OR MELANOMA OR CARCINOMA OR GLIOMA OR MYELOMA OR NE- OPLASM OR NEOPLASTIC
S5	3774	S1 AND S4
S6	32876	S1/TI
S7	2015394	S4/TI
S8	68	S6 AND S7
S9	37	RD (unique items)
S10	26277	S2 OR S3
S11	26277	S10/I
S12	9552	S10/TI
S13	74	S12 AND S7
S14	30	RD (unique items)
S15	28	S14 NOT S9
S16	38725	GREEN (W) FLUORESCENT (W) PROTEIN
S17	135016	GALACTOSIDASE
S18	170051	S16 OR S17
S19	1037776	RECOMBINANT?
S20	154508	GENE (W) THERAPY
S21	1149213	S19 OR S20
S22	1865	S1 AND S21 AND S4
S23	786	S18 AND S22
S24	536	S23 NOT PY>2000
S25	536	RD (unique items)
S26	1621	S1(S)S4
S27	168	S26 AND S25
S28	35202	S18/TI
S29	35	S28 AND S6
S30	34	S29 NOT PY>2000
S31	6	RD (unique items)
S32	3	EDMONSTRON (5N) ZAGREB
S33	3	S32 NOT PY>2000
S34	4	EDMONSTRON AND ZAGREB
S35	1	S34 NOT S33
S36	0	EDMONSTRON (S) ENDERS
S37	1477	ENDERS
S38	104	S1(S)S37
S39	203	MORATEN
S40	0	S1(S)S40
S41	0	S S1(S)S39
S42	203	S1 AND S39
S43	745	BERNA
S44	61	S1 AND S43
S45	0	S38 AND S42 AND S44
S46	334	S38 OR S42 OR S44
S47	304	S46 NOT PY>2000
S48	164	RD (unique items)
S49	83958	POINT (W) MUTATION
S50	107	ATTENUVAX
S51	8265	MMR
S52	45	PRIORIX
S53	101	S50 NOT PY>2000
S54	7047	S51 NOT PY>2000
S55	36	S52 NOT PY>2000
S56	1628	ZAGREB/TI
S57	15	S56 AND S46
S58	133	ENDERS/TI
S59	10	S48 AND S58
S60	67550843	A

## DIALOG

S61 178 BERNA/TI  
S62 2 S48 AND S61  
S63 11 S48 AND S49  
S64 11 S63 NOT PY>2000  
S65 11 RD (unique items)  
S66 101 S50 NOT PY>2000  
S67 71 RD (unique items)  
S68 36 S52 NOT PY>2000  
S69 19 RD (unique items)  
S70 0 S67 AND S69  
S71 486 E1P  
S72 539 AU="RUSSELL S"  
S73 200 AU="RUSSELL S J"  
S74 1 AU="RUSSELL S.J."  
S75 152 AU="RUSSELL S.J."  
S76 176 AU="FIELDING A" OR AU="FIELDING A."  
S77 86 AU="PENG K"  
S78 29 AU="PENG K." OR AU="PENG K.-W."  
S79 54 AU="GROTE D"  
S80 3 AU="GROTE DEANNA"  
S81 1217 S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80  
S82 15 S81 AND (S1 OR S2 OR S3) AND S4  
S83 10 RD (unique items)  
S84 7 S83 NOT PY>2000  
?

9/3,AB/1 (Item 1 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

11674780 21452778 PMID: 11567982

**Systemic therapy of myeloma xenografts by an attenuated measles virus.**

Peng KW; Ahmann GJ; Pham L; Greipp PR; Cattaneo R; Russell SJ  
Molecular Medicine Program and the Department of Hematology, Mayo Foundation, Rochester, MN.

Blood (United States) Oct 1 2001, 98 (7) p2002-7, ISSN 0006-4971  
Journal Code: A8G

Languages: ENGLISH

Document type: Journal Article

Record type: In Process

Conditionally replicating viruses are promising agents for the treatment of malignancy. Here it is shown that the live attenuated Edmonston-B vaccine strain of measles virus (MV-Edm) replicates selectively in human myeloma cells and has potent antitumor activity. In vitro, replication of MV-Edm was restricted in phytohemagglutinin (PHA)-stimulated peripheral blood lymphocytes (PBLs) but proceeded efficiently in a panel of 6 myeloma cell lines-ARH-77, RPMI 8226, JJN-3, MM1, KAS-6/1, and KMS-11-and in primary myeloma cells isolated by CD138 sorting from the bone marrow aspirates of 6 patients. MV-Edm infection induced potent cytopathic effects in these myeloma cells, resulting in the formation of multinucleated syncytia that eventually became nonviable. In contrast, syncytial formation in PHA-stimulated PBLs was minimal after MV-Edm infection. In vivo, MV-Edm was antitumorigenic and inhibited the establishment of myeloma cells as xenografts in immunocompromised mice. When injected directly into ARH-77 myeloma xenografts in the mice, MV-Edm caused complete regression of these xenografts. MV-Edm administered intravenously into the tail veins of mice also showed significant antineoplastic activity against established RPMI 8226 and ARH-77 xenografts. In particular, the ARH-77 myeloma xenografts were exquisitely sensitive to MV-Edm therapy, and tumors in all mice regressed completely. In light of its selectivity for myeloma cells and its potent antineoplastic activity against myeloma xenografts in vivo, MV-Edm merits further development for the treatment of multiple myeloma. (Blood. 2001;98:2002-2007)

9/3,AB/2 (Item 2 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

11674774 21452772 PMID: 11567976

**Myeloma gets the measles.**

Dunbar CE

National Institutes of Health.

Blood (United States) Oct 1 2001, 98 (7) p1999, ISSN 0006-4971  
Journal Code: A8G

Languages: ENGLISH

Document type: Journal Article

Record type: In Process

9/3,AB/3 (Item 3 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

11568085 21406255 PMID: 11513988

**Measles vaccine treats cancer.**

Davies MJ

Trends in biotechnology (England) Sep 2001, 19 (9) p332-3, ISSN 0167-7799  
Journal Code: ALJ

Languages: ENGLISH

Document type: Journal Article  
Record type: In Process

9/3,AB/13 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13105373 BIOSIS NO.: 200100312522

**Engineering measles virus as an oncolytic agent for the treatment of multiple myeloma.**

AUTHOR: Peng Kah-Whye(a); Donovan Kathleen(a); Zhang Jie(a); Schneider Urs(a); Lust John(a); Cattaneo Roberto(a); Russell Stephen J(a)

AUTHOR ADDRESS: (a)Mayo Foundation, Rochester, MN\*\*USA

JOURNAL: Blood 96 (11 Part 1):p512a November 16, 2000

MEDIUM: print

CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000

SPONSOR: American Society of Hematology

ISSN: 0006-4971

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:** A variety of oncolytic viruses have shown promise for tumor therapy. Ideally, the virus should be potentially toxic to target cells but cause limited damage to normal tissues. We demonstrate here that a previously unexplored agent, the Edmonston B vaccine strain of measles virus (MV-Edm), has anti-neoplastic activity against large human multiple myeloma xenografts and that the virus can be engineered to enter and spread in susceptible cells in a receptor dependent way. MV-Edm infected and replicated efficiently in ARH-77 and RPMI 8226 myeloma cell lines, causing massive cell-cell fusion and formation of multinucleated syncytia. On non-transformed lymphocytes, the replicative spread of the virus was at least 100-fold less efficient. When administered intratumorally into established multiple myeloma xenografts in immunocompromised mice, MV-Edm repressed the growth of all treated tumors. MV-Edm was most potent against the ARH-77 myeloma xenografts. When delivered intravenously as a single dose or multiple doses, MV-Edm caused complete regression of all of the ARH-77 myeloma xenografts. To generate an engineered MV suitable for targeted myeloma therapy, a single chain antibody fragment (scFv) to a myeloma cell surface antigen, CD38, was generated. A scFv generated against CD52, a lymphocyte antigen, was generated as a control. The respective scFvs were fused to the C-terminus of the MV-H glycoprotein. The recombinant viruses replicated as efficiently as the standard virus on Vero African green monkey kidney cells indicating that they retained their ability to mediate infection through CD46 (natural receptor for measles virus). The targeting properties of the recombinant viruses were tested on parental CHO cells (CD46 negative) or CD38-expressing CHO cells. Standard and alpha-CD52 MV viruses were unable to infect CHO or CD38-CHO cells. The alpha-CD38 MV infected and replicated efficiently in CD38-CHO cells inducing cell-cell fusion and cell death. Infectivity on the CD38-CHO cells was ablated by proteolytic removal of the scFv. MV-Edm merits further study as a novel therapeutic agent for the treatment of multiple myeloma.

2000

9/3,AB/18 (Item 6 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2001 BIOSIS. All rts. reserv.

03304593 BIOSIS NO.: 000072032697

**THERAPY OF MAMMARY CARCINOMA OF C-3H MICE BY MEANS OF THYMIC FACTOR  
MEASLES VACCINE AND L DOPA**

AUTHOR: BUSSE E; ROSE H; HELMHOLZ M

AUTHOR ADDRESS: GESCHWULSTKLINIK DER CHARITE, ABTEILUNG FUER ANGEWANDTE  
TUMORBIOL., DDR - 1040 BERLIN, SCHUMANNSTR. 20/21.

JOURNAL: RADIOBIOL RADIOTHER 22 (1). 1981. 63-68. 1981

FULL JOURNAL NAME: Radiobiologia Radiotherapia

CODEN: RDBGA

RECORD TYPE: Abstract

LANGUAGE: GERMAN

ABSTRACT: C3H mice with spontaneous mammary tumors were treated with thymus hormone, L-dopa and measles vaccine [immunotherapy]. In 63% of the tumor carriers a regression of the carcinoma could be achieved. The thymic factor was obtained from calf thymus and was not species-specific.

1981

**9/3,AB/22 (Item 1 from file: 34)**

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

(c) 2001 Inst for Sci Info. All rts. reserv.

10087236 Genuine Article#: 476KC Number of References: 0

**Title: A trackable vaccine strain of measles virus for intraperitoneal  
therapy of ovarian cancer.**

Author(s): TenEyck C; Galanis E; Kalli K; Hartmann L; Russell SJ; Peng KW

Corporate Source: Mayo Clin & Mayo Fdn,Rochester//MN/55905; Mayo Clin &

Mayo Fdn,Endocrine Res Unit,Rochester//MN/55905

Journal: GENE THERAPY, 2001, V8, 1 (OCT), PS12-S12

ISSN: 0969-7128 Publication date: 20011000

Publisher: NATURE PUBLISHING GROUP, HOUNDMILLS, BASINGSTOKE RG21 6XS,  
HAMPSHIRE, ENGLAND

Language: English Document Type: MEETING ABSTRACT

**9/3,AB/24 (Item 2 from file: 73)**

DIALOG(R)File 73:EMBASE

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01918653 EMBASE No: 1981097817

**On the therapy of mammary carcinoma of C3H mice by means of thymic  
factor, measles vaccine and L-dopa**

ZUR THERAPIE DES MAMMA-KARZINOMS VON C3H-MAUSEN MITTELS THYMUSFAKTOR,  
MASERNVAKZINE UND L-DOPA

Busse E.; Rose H.; Helmholtz M.

Geschwulstklin., Ber. Med., Humboldt-Univ., 1040 Berlin Germany

Radiobiologia Radiotherapia ( RADIOBIOL. RADIOTHER. ) (Germany) 1981,  
22/1 (63-68)

CODEN: RDBGA

DOCUMENT TYPE: Journal

LANGUAGE: GERMAN SUMMARY LANGUAGE: RUSSIAN; ENGLISH

C3H mice with spontaneously developed mammary tumours were treated with thymic hormone, L-dopa and measles vaccine. In 63% of the tumour carriers are regression of the mammary carcinoma could be achieved. The thymic factor was obtained from calf thymus and was not species-specific.

**9/3,AB/28 (Item 1 from file: 357)**

DIALOG(R)File 357:Derwent Biotechnology Abs

(c) 2001 Derwent Publ Ltd. All rts. reserv.

0269750 DBA Accession No.: 2001-09504

**Live attenuated measles virus induces regression of human lymphoma xenografts in immunodeficient mice- vector-mediated beta-galactosidase reporter gene transfer, expression in tumor cell, transplantation in mouse and Vero cell packaging cell culture for nucleic acid vaccine and cancer gene therapy**

AUTHOR: Grote D; Russell S J; Cornu T I; Cattaneo R; Vile R; Poland G A; +Fielding A K

CORPORATE AFFILIATE: Mayo-Clin.Rochester Univ.Zurich-Inst.Mol.Biol.

CORPORATE SOURCE: Mayo Clinic, Guggenheim 18, 200 1st St, SW, Rochester, MN 55905, USA. email:adele.fielding@mayo.edu

JOURNAL: Blood (97, 12, 3746-54) 2001

ISSN: 0006-4971 CODEN: BLOOAW

LANGUAGE: English

**ABSTRACT:** Live attenuated measles virus (MV) that induce regression of human lymphoma xenografts in immunodeficient mice were evaluated. MV (unmodified MV-Ed or modified MV-Ed containing beta-galactosidase (EC-3.2.1.23) reporter gene) was inoculated onto 10(6) Vero cells in T75 tissue culture flasks at a MOI of 0.01 in 2 ml Optimem at 37 deg for 2 hr. The virus inoculum was removed and replaced by normal medium. The cultures were then observed until all cells were harvested in 2 ml Optimem and the virus was released by 2 cycles of freeze-thawing. DoHH2 cells and Raji cells (ATCC CCL-86) were infected with MV at an MOI of 0.01. Mice (4 wk old Balb/C SCID) were injected s.c. in the flank region with 10(7) viable tumor cells. For intratumoral administration, after the tumors reached a volume of about 0.4 cm cub., they were injected daily with MV in a total volume of 100 ul for 10 days. For i.v. administration, the mice were injected with 1 x 10(7) pfu MV via the tail vein on 4 occasions. The attenuated virus vaccine mediated regression of large, established B-lymphocyte xenografts in SCID mice, and proved that MV is oncolytic for lymphomas in vivo. (37 ref)

9/3,AB/30 (Item 3 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs

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0243877 DBA Accession No.: 1999-14642

**Use of fusogenic membrane glycoproteins as novel therapeutic transgenes in gliomas- measles virus and gibbon-ape-leukemia virus glycoprotein gene transfer by retro virus, adeno virus or plasmid vector for potential glioma gene therapy (conference abstract)**

AUTHOR: Galanis E; Vile R; James C D; Russell S J

CORPORATE AFFILIATE: Mayo-Clin.Rochester

CORPORATE SOURCE: Mayo Clinic, Rochester, MN 55905, USA.

JOURNAL: Gene Ther. (6, Suppl.1, S7) 1999

ISSN: 0969-7128 CODEN: GETHEC

CONFERENCE PROCEEDINGS: Cytoreductive Gene Therapy Harold W. Siebens Conference, Phillips Hall, Siebens Medical Education Building, Mayo Foundation, Rochester, MN, USA, 25-27 September, 1999.

LANGUAGE: English

**ABSTRACT:** Virus fusogenic membrane glycoproteins from measles virus (MV), MV glycoprotein-H and MV glycoprotein-F and a mutated form of the retro virus envelope protein of gibbon-ape-leukemia virus (GALV.fus) were used as therapeutic transgenes for glioma therapy. The U87 and U118 glioma cell lines were stably transduced with the LacZ gene allowing direct formation after staining with x-gal. The MV glycoprotein-F and -H cDNAs were cloned into plasmid pCG vector and GALV.fus cDNA was cloned into plasmid pCR3.1 vector. Co-transfection of the U87 and U118 cells with MV-F and MV-H lead in 48 hr to complete replacement of monolayer culture by syncytia followed by massive cell death in 5-6 days. Transfection by MV-F or MV-H alone did not give cytopathic

effect. Cytotoxicity in the U87 and U118 cell lines was higher than the cytotoxicity caused by transfection with herpes simplex virus thymidine-kinase (EC-) gene followed by ganciclovir treatment. Similar results were obtained with GALV.fus. The bystander effect in glioma cell lines was high. Adeno virus and bicistronic retro viruses will be produced. (0 ref)

9/3,AB/31 (Item 4 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs  
(c) 2001 Derwent Publ Ltd. All rts. reserv.

0243871 DBA Accession No.: 1999-14636

**Redirecting measles virus hemagglutinin (H) protein to cancerous cells-  
surface display of carcinoembryonic antigen-specific single chain  
antibody on measles virus for use as gene therapy vector for cancer  
therapy (conference abstract)**

AUTHOR: Murphy A L; Zhang J; Russell S J; Cattaneo R

CORPORATE AFFILIATE: Mayo-Clin.Rochester

CORPORATE SOURCE: Molecular Medicine Program, Mayo Clinic, Rochester, MN  
55905, USA.

JOURNAL: Gene Ther. (6, Suppl.1, S4) 1999

ISSN: 0969-7128 CODEN: GETHEC

CONFERENCE PROCEEDINGS: Cytoeductive Gene Therapy Harold W. Siebens  
Conference, Phillips Hall, Siebens Medical Education Building, Mayo  
Foundation, Rochester, MN, USA, 25-27 September, 1999.

LANGUAGE: English

ABSTRACT: To attempt to retarget measles virus (MV) to cancer cells, a single chain antibody (scAb) specific for carcinoembryonic antigen (CAE) (a cancer-associated membrane glycoprotein) was displayed as a C-terminal fusion of the MV attachment protein, hemagglutinin (H). 3 Forms of the scAb were displayed with linker lengths of 0, 5, and 15 amino acids separating VH and VL domains. The H protein modified with the long linker scAb mediated cell-cell fusion preferentially in HeLa cells overexpressing CEA. The specificity of this interaction and its dependence on CEA was assessed. Most 0 and 5 amino acid linker scAb-H fusions lost the ability to mediate syncytium formation in HeLa and HeLa-CEA cells, possibly due to oligomerization causing steric hindrance. N-terminal display of these scAbs formed on a retro virus envelope protein showed that the short and zero linkers formed oligomers which inhibited virus-induced fusion. The longer linker scAb may act to positively redirect MV entry. This hybrid H protein is being built into a replication competent MV and further studies concerning its ability to retarget the virus to CEA-expressing cells were presented. (0 ref)

9/3,AB/32 (Item 5 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs  
(c) 2001 Derwent Publ Ltd. All rts. reserv.

0219388 DBA Accession No.: 98-00985 PATENT

**Polycistronic expression plasmid encoding one or more viral antigens for  
cancer immunotherapy- measles virus, rubella virus,  
varicella-zoster virus, herpes virus or hepatitis B virus antigen gene  
transfer, and cytokine-mediated gene therapy**

AUTHOR: Boehm W; Shirmbeck R; Reimann J

CORPORATE SOURCE: Brunswick, Germany.

PATENT ASSIGNEE: Ges.Biotechnol.Forsch. 1997

PATENT NUMBER: EP 805207 PATENT DATE: 971105 WPI ACCESSION NO.: 97-529061  
(9749)

PRIORITY APPLIC. NO.: EP 96106935 APPLIC. DATE: 960502

NATIONAL APPLIC. NO.: EP 966935 APPLIC. DATE: 960502

DIALOG

LANGUAGE: English

ABSTRACT: A new polycistronic expression plasmid encodes one or more viral antigens suitable for DNA-based immunization of a cancer-bearing patient, and transfection in vitro and in vivo of tumor cells. Also claimed are tumor cells, which are transfected in vitro with a plasmid for injection into the patient. The plasmid may also encode 1 or more cytokines and encodes 1 or more antigens of a common viral pathogen, e.g. measles virus, rubella virus, varicella-zoster virus, herpes virus or hepatitis B virus. The plasmid is produced by screening for specific T-cell reactivity directed against 1 or more viral antigens in peripheral blood from a cancer-bearing heart patient in vitro, and cloning one or more of the viral antigens, and optionally one or more cytokines, into a polycistronic expression vector. The plasmid may be used for cancer immunotherapy by injecting the plasmid into tumor cells in vivo, or by isolating and transfecting tumor cells from a patient in vitro for reinjection. (20pp)

9/3,AB/33 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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94041258 CA: 94(7)41258z JOURNAL

Effect of cAMP and interferon level in the lymphocytes and change in the rate of tumor growth of a transplantable melanoma of golden hamster by the treatment of the experimental animals with BCG, measles vaccine and L-dopa and amantadin

AUTHOR(S): Busse, E.; Rose, H.; Riessbeck, K. H.

LOCATION: Geschwulstklin., Humboldt-Univ., Berlin, Ger. Dem. Rep.

JOURNAL: Radiobiol., Radiother. DATE: 1980 VOLUME: 21 NUMBER: 3

PAGES: 292-301 CODEN: RDBGAT ISSN: 0033-8184 LANGUAGE: German

?



27/3,AB/1 (Item 1 from file: 399)  
 DIALOG(R)File 399:CA SEARCH(R)  
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133250614 CA: 133(18)250614a JOURNAL  
**In vitro and in vivo infection of neural cells by a recombinant measles virus expressing enhanced green fluorescent protein**  
 AUTHOR(S): Duprex, W. Paul; McQuaid, Stephen; Roscic-Mrkic, Branka; Cattaneo, Roberto; McCallister, Cecilia; Rima, Bert K.  
 LOCATION: School of Biology and Biochemistry, The Queen's University of Belfast, Belfast, UK, BT9 7BL  
 JOURNAL: J. Virol. DATE: 2000 VOLUME: 74 NUMBER: 17 PAGES: 7972-7979  
 CODEN: JOVIAM ISSN: 0022-538X LANGUAGE: English PUBLISHER: American Society for Microbiology

27/3,AB/23 (Item 20 from file: 349)  
 DIALOG(R)File 349:PCT FULLTEXT  
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00450028  
**COMPOSITIONS AND METHODS FOR ELIMINATION OF UNWANTED CELLS**  
**COMPOSITIONS ET METHODES D'ELIMINATION DE CELLULES INDESIRABLES**  
 Patent Applicant/Assignee:  
 MEDICAL RESEARCH COUNCIL,  
 RUSSELL Stephen James,  
 MORLING Frances Joanne,  
 FIELDING Adele Kay,  
 COSSET Francois-Loic,  
 CATTANEO Roberto,  
 Inventor(s):  
 RUSSELL Stephen James,  
 MORLING Frances Joanne,  
 FIELDING Adele Kay,  
 COSSET Francois-Loic,  
 CATTANEO Roberto,  
 Patent and Priority Information (Country, Number, Date):  
 Patent: WO 9840492 A1 19980917  
 Application: WO 98GB710 19980310 (PCT/WO GB9800710)  
 Priority Application: GB 975007 19970311; US 9745164 19970430  
 Designated States: AU CA JP US AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
 Publication Language: English  
 Fulltext Word Count: 9525

#### English Abstract

Disclosed is a **recombinant** nucleic acid vector for use in **gene therapy** of malignant disease, the vector directing the expression on a eukaryotic cell surface of a syncytium-inducing polypeptide.

#### French Abstract

L'invention concerne un vecteur d'acide nucleique recombine destine a etre utilise dans une therapie genique d'affection maligne, le vecteur dirigeant l'expression sur une surface de cellule eucaryote d'un polypeptide induisant le syncytium.

27/3,AB/79 (Item 44 from file: 654)  
 DIALOG(R)File 654:US PAT.FULL.  
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03067812

Utility

**MEASLES VIRUS PEPTIDES WITH ANTIFUSOGENIC AND ANTIVIRAL ACTIVITIES**  
[ As inhibitory of human and non-human retroviral, especially human immunodeficiency viurs (HIV), transmission to uninfected cells]

PATENT NO.: 6,013,263  
ISSUED: January 11, 2000 (20000111)  
INVENTOR(s): Barney, Shawn O'Lin, Cary, NC (North Carolina), US (United States of America)  
Lambert, Dennis Michael, Cary, NC (North Carolina), US (United States of America)  
Petteway, Stephen Robert, Cary, NC (North Carolina), US (United States of America)  
ASSIGNEE(s): Trimeris, Inc , (A U.S. Company or Corporation), Durham, NC (North Carolina), US (United States of America)  
[Assignee Code(s): 52157]  
APPL. NO.: 8-486,099  
FILED: June 07, 1995 (19950607)

This is a division, of application Ser. No. 08-470,896, filed Jun. 6, 1995 is a Continuation-In-Part of Ser. No. 08-360,107 filed Dec. 20, 1994, which is a Continuation-In-Part of Ser. No. 08-255,208 filed Jun. 7, 1994, which is a Continuation-In-Part of Ser. No. 08-073,028 filed Jun. 7, 1993, now U.S. Pat. No. 5,464,933, each of which is incorporated herein by reference in its entirety.

This invention was made with Government support under Grant No. AI-30411-02 awarded by the National Institutes of Health. The Government has certain rights in the invention.

FULL TEXT: 44235 lines

#### ABSTRACT

The present invention relates to peptides which exhibit potent anti-retroviral activity. The peptides of the invention comprise DP178 (SEQ ID:1) peptide corresponding to amino acids 638 to 673 of the HIV-1 sub LAI gp41 protein, and fragments, analogs and homologs of DP178. The invention further relates to the uses of such peptides as inhibitory of human and non-human retroviral, especially HIV, transmission to uninfected cells.  
?

31/3,AB/1 (Item 1 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10717752 20392151 PMID: 10933705

**In vitro and in vivo infection of neural cells by a recombinant measles virus expressing enhanced green fluorescent protein.**

Duprex WP; McQuaid S; Roscic-Mrkic B; Cattaneo R; McCallister C; Rima BK  
School of Biology and Biochemistry, The Queen's University of Belfast,  
Belfast BT9 7BL, Northern Ireland, United Kingdom. p.duprex@qub.ac.uk

Journal of virology (UNITED STATES) Sep 2000, 74 (17) p7972-9,  
ISSN 0022-538X Journal Code: KCV

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

This study focused on the in vitro infection of mouse and human neuroblastoma cells and the in vivo infection of the murine central nervous system with a recombinant measles virus. An undifferentiated mouse neuroblastoma cell line (TMN) was infected with the vaccine strain of measles virus (MVeGFP), which expresses enhanced green fluorescent protein (EGFP). MVeGFP infected the cells, and cell-to-cell spread was studied by virtue of the resulting EGFP autofluorescence, using real-time confocal microscopy. Cells were differentiated to a neuronal phenotype, and extended processes, which interconnected the cells, were observed. It was also possible to infect the differentiated neuroblastoma cells (dTMN) with MVeGFP. Single autofluorescent EGFP-positive cells were selected at the earliest possible point in the infection, and the spread of EGFP autofluorescence was monitored. In this instance the virus used the interconnecting processes to spread from cell to cell. Human neuroblastoma cells (SH-SY-5Y) were also infected with MVeGFP. The virus infected these cells, and existing processes were used to initiate new foci of infection at distinct regions of the monolayer. Transgenic animals expressing CD46, a measles virus receptor, and lacking interferon type 1 receptor gene were infected intracerebrally with MVeGFP. A productive infection ensued, and the mice exhibited clinical signs of infection, such as ataxia and an awkward gait, identical to those previously observed for the parental virus (Edtag). Mice were sacrificed, and brain sections were examined for EGFP autofluorescence by confocal scanning laser microscopy over a period of 6 h. EGFP was detected in discrete focal regions of the brain and in processes, which extended deep into the parenchyma. Collectively, these results indicate (i) that MVeGFP can be used to monitor virus replication sensitively, in real time, in animal tissues, (ii) that infection of ependymal cells and neuroblasts provides a route by which measles virus can enter the central nervous system in mouse models of encephalitis, and (iii) that upon infection, the virus spreads transneuronally.

31/3,AB/2 (Item 2 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10370819 99445864 PMID: 10516065

**Observation of measles virus cell-to-cell spread in astrocytoma cells by using a green fluorescent protein-expressing recombinant virus.**

Duprex WP; McQuaid S; Hangartner L; Billeter MA; Rima BK  
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Belfast BT9 7BL, Northern Ireland, United Kingdom. p.duprex@qub.ac.uk

Journal of virology (UNITED STATES) Nov 1999, 73 (11) p9568-75,  
ISSN 0022-538X Journal Code: KCV

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

A recombinant measles virus (MV) which expresses enhanced green fluorescent protein (EGFP) has been rescued. This virus, MVeGFP, expresses

the reporter gene from an additional transcription unit which is located prior to the gene encoding the measles virus nucleocapsid protein. The recombinant virus was used to infect human astrocytoma cells (GCCM). Immunocytochemistry (ICC) together with EGFP autofluorescence showed that EGFP is both an early and very sensitive indicator of cell infection. Cells that were EGFP-positive and ICC-negative were frequently observed. Confocal microscopy was used to indirectly visualize MV infection of GCCM cells and to subsequently follow cell-to-cell spread in real time. These astrocytoma cells have extended processes, which in many cases are intimately associated. The processes appear to have an important role in cell-to-cell spread, and MVeGFP was observed to utilize them in the infection of surrounding cells. Heterogeneity was seen in cell-to-cell spread in what was expected to be a homogeneous monolayer. In tissue culture, physical constraints govern the integrity of the syncytia which are formed upon extensive cell fusion. When around 50 cells were fused, the syncytia rapidly disintegrated and many of the infected cells detached. Residual adherent EGFP-positive cells were seen to either continue to be involved in the infection of surrounding cells or to remain EGFP positive but no longer participate in the transmission of MV infection to neighboring cells.

31/3,AB/5 (Item 1 from file: 71)  
 DIALOG(R)File 71:ELSEVIER BIOBASE  
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01516001 2000189962

**In vitro and in vivo infection of neural cells by a recombinant measles virus expressing enhanced green fluorescent protein**

Paul Duprex W.; McQuaid S.; Roscic-Mrkic B.; Cattaneo R.; McCallister C.; Rima B.K.

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Journal: Journal of Virology, 74/17 (7972-7979), 2000, United States

CODEN: JOVIA

ISSN: 0022-538X

DOCUMENT TYPE: Article

LANGUAGES: English SUMMARY LANGUAGES: English

NO. OF REFERENCES: 47

This study focused on the in vitro infection of mouse and human neuroblastoma cells and the in vivo infection of the murine central nervous system with a recombinant measles virus. An undifferentiated mouse neuroblastoma cell line (TMN) was infected with the vaccine strain of measles virus (MVeGFP), which expresses enhanced green fluorescent protein (EGFP). MVeGFP infected the cells, and cell-to-cell spread was studied by virtue of the resulting EGFP autofluorescence, using real-time confocal microscopy. Cells were differentiated to a neuronal phenotype, and extended processes, which interconnected the cells, were observed. It was also possible to infect the differentiated neuroblastoma cells (dTMN) with MVeGFP. Single autofluorescent EGFP-positive cells were selected at the earliest possible point in the infection, and the spread of EGFP autofluorescence was monitored. In this instance the virus used the interconnecting processes to spread from cell to cell. Human neuroblastoma cells (SH-SY-5Y) were also infected with MVeGFP. The virus infected these cells, and existing processes were used to initiate new foci of infection at distinct regions of the monolayer. Transgenic animals expressing CD46, a measles virus receptor, and lacking interferon type 1 receptor gene were infected intracerebrally with MVeGFP. A productive infection ensued, and the mice exhibited clinical signs of infection, such as ataxia and an awkward gait, identical to those previously observed for the parental virus (Edtag). Mice were sacrificed, and brain sections were examined for EGFP

autofluorescence by confocal scanning laser microscopy over a period of 6 h. EGFP was detected in discrete focal regions of the brain and in processes, which extended deep into the parenchyma. Collectively, these results indicate (i) that MVeGFP can be used to monitor virus replication sensitively, in real time, in animal tissues, (ii) that infection of ependymal cells and neuroblasts provides a route by which measles virus can enter the central nervous system in mouse models of encephalitis, and (iii) that upon infection, the virus spreads transneuronally.

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57/3,AB/1 (Item 1 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

09575478 97406832 PMID: 9260214

**Measles vaccine in egg allergic children: poor immunogenicity of the Edmonston- Zagreb strain.**

Bruno G; Grandolfo M; Lucenti P; Novello F; Ridolfi B; Businco L

Department of Pediatrics, University of Rome La Sapienza, Italy.

Pediatric allergy and immunology (DENMARK) Feb 1997, 8 (1) p17-20,  
ISSN 0905-6157 Journal Code: BU6

Languages: ENGLISH

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial

Record type: Completed

Despite the fact that a number of recent studies have shown that **measles** / mumps/rubella vaccine is safe for egg allergic children, many pediatricians are still concerned about immunization in egg allergic children. In Europe, a **measles** vaccine with the Edmonston-Zagreb strain (EZMV) grown in human fibroblast culture has been developed and recommended for children with egg allergy. However, some doubt arises on the efficacy of this strain due to its weak immunogenicity. The aim of this study was to investigate the immunogenicity of the EZMV in comparison to the **measles** vaccine with the Schwarz strain (SWMV) grown in a chick embryo fibroblast culture. Thirty-nine children affected by severe immediate manifestations due to IgE mediated egg allergy were enrolled. The children received at random the SWMV (Morupar, Sclavo) or the EZMV (Triviraten, Berna) in one 0.5 ml subcutaneous injection, and were checked for any immediate allergic reactions in the following 4 hours. Blood samples were taken for the detection of specific antibody response 5 months after the immunization. In SWMV seroconverted children (18/19) the geometric mean antibody titer was 3 times higher than that observed in EZMV seroconverted children (17/20) (p < 0.01). No allergic reactions occurred following the immunization with the two different vaccines. This data confirms the safety of SWMV in egg allergic children. In addition, the present study provides further data on the lower immunogenicity of the EZMV in comparison to the SWMV.

57/3,AB/2 (Item 2 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

08241444 94378708 PMID: 8091849

**Infection of leucocytes by measles vaccine viruses Edmonston- Zagreb and Enders- Moraten has different consequences: potential mechanism for increased vaccine efficacy or aberrant activity in field trials.**

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Department of Microbiology and Immunology, Baylor College of Medicine, Houston, TX 77030.

Vaccine (ENGLAND) Jun 1994, 12 (8) p715-22, ISSN 0264-410X  
Journal Code: X60

Contract/Grant No.: NO1-AI 82509, AI, NIAID

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The abilities of two **measles** vaccine virus strains, Edmonston-Zagreb (E-Z) and **Enders -Moraten** (E-M), to infect and modify the activities of U937 monocytoid and peripheral blood mononuclear leucocytes (PBMLs) were compared with each other and with changes resulting from infection of these cells by a wild-type **measles** virus (MV). Both the E-Z and wild-type MV were shown to infect U937 and PBMLs and (1) to markedly increase expression of leucocyte function antigen 1 (LFA-1) on leucocytes present in infected cultures; (2) to increase cell-cell interaction; (3) to grow and disseminate readily in both types of leucocyte cultures; and (4) to persist for more than 7 days in these cultures despite the presence of MV-specific

neutralizing antibodies. In contrast, the E-M virus did not grow well in unstimulated PBMLs and, although it did grow well in U937 cells, it did not noticeably alter the expression of LFA-1 on these cells, did not induce significant cell-cell interaction, and was rapidly eliminated from these cultures if MV-specific neutralizing antibodies were present. The possible relationship of these findings to the increased protective efficacy and untoward effects associated with the E-Z MV vaccine is discussed.

57/3,AB/4 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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09355094 BIOSIS NO.: 199497363464

**Infection of leukocytes by measles vaccine viruses Edmonston- Zagreb and Enders- Moraten has different consequences: Potential mechanism for increased vaccine efficacy or aberrant activity in field trials.**

AUTHOR: Wyde Philip R(a); Attibele Nagendra R; Kemp Walter L

AUTHOR ADDRESS: (a)Dep. Microbiol. Immunol., Baylor Coll. Med., 1 Baylor Plaza, Houston, TX 77030\*\*USA

JOURNAL: Vaccine 12 (8):p715-722 1994

ISSN: 0264-410X

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

**ABSTRACT:** The abilities of two measles vaccine virus strains, Edmonston-Zageb (E-Z) and **Enders -Moraten** (E-M), to infect and modify the activities of U937 monocytoid and peripheral blood mononuclear leucocytes (PBMLs) were compared with each other and with changes resulting from infection of these cells by a wild-type measles virus (MV). Both the E-Z and wild-type MV were shown to infect U937 and PBMLs and (1) to markedly increase expression of leucocyte function antigen 1 (LFA-1) on leucocytes present in infected cultures; (2) to increase cell-cell interaction; (3) to grow and disseminate readily in both types of leucocyte cultures; and (4) to persist for more than 7 days in these cultures despite the presence of MV-specific neutralizing antibodies. In contrast, the EE-M virus did not grow well in unstimulated PBMLs and, although it did grow well in U937 cells it did not noticeably alter the expression of LFA-1 on these cells, did not induce significant cell-cell interaction, and was rapidly eliminated from these cultures if MV-specific neutralizing antibodies were present. The possible relationship of these findings to the increased protective efficacy and untoward effects associated with the E-Z MV vaccine is discussed.

1994

57/3,AB/5 (Item 3 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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08418693 BIOSIS NO.: 000043115272

**SEROLOGIC RESPONSE TO EDMONSTON- ZAGREB AND MORATEN MEASLES VACCINE UNITED STATES**

AUTHOR: MARKOWITZ L E; DEMONTEVERDE R; ALBRECHT P; POWELL C; SWINT E;

PATRIARCA P; KAISER MEASLES VACCINE STUDY GROUP (USA)

AUTHOR ADDRESS: CDC, ATLANTA, GA.

JOURNAL: 32ND INTERSCIENCE CONFERENCE ON ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, ANAHEIM, CALIFORNIA, USA, OCTOBER 11-14, 1992. PROGRAM ABSTR INTERSCI CONF ANTIMICROB AGENTS CHEMOTHERAPY 32 (0). 1992. 180. 1992

CODEN: POCH

DOCUMENT TYPE: Meeting

DIALOG

RECORD TYPE: Citation  
LANGUAGE: ENGLISH  
1992  
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 DIALOG(R)File 5:BIOSIS Previews(R)  
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13114832 BIOSIS NO.: 200100321981

**Live attenuated measles virus as a replicating virus therapy for non-Hodgkin's lymphoma.**

AUTHOR: Grote Deanna (a); Cornu Tatjana; Cattaneo Roberto(a); Russell Stephen(a); Fielding Adele(a)

AUTHOR ADDRESS: (a)Molecular Medicine Program, Mayo Foundation, Rochester, MN\*\*USA

JOURNAL: Blood 96 (11 Part 1):p212a November 16, 2000

MEDIUM: print

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SPONSOR: American Society of Hematology

ISSN: 0006-4971

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:** There is increasing interest in the use of replicating viruses in the therapy of human cancer . We have studied the Edmonston (vaccine) strain of the human paramyxovirus, **measles** , as a potential replicating virus therapy for B cell lymphomas. The natural tropism of **measles** virus (MV) to replicate within lymphoid tissue combined with the availability of a safe, live attenuated vaccine strain make this virus an ideal candidate for the 'virotherapy' of B cell malignancies. We used as our lymphoma model subcutaneously implanted human tumors xenografts (DoHH2 and Raji cells, which express equivalent numbers of the MV receptor, CD46) in immunodeficient (SCID) mice. We confirmed that MV was able to replicate lytically within these cell lines. We then showed that intratumoral injection of 10 doses of either MV-Edmonston or a genetically modified MV-Edmonston expressing beta-galactosidase, at a titre of between 10<sup>5</sup> and 10<sup>6</sup> in a volume of 100 µl resulted in regression of large established human DoHH2 or Raji xenografts. In some cases, complete tumor regression was observed. No such effect was observed after injection of a control UV-inactivated MV. Analysis of residual tumors, where applicable, showed that in some cases, the characteristic cytopathic effects of MV infection, the formation of multinucleated syncytia could be observed. We were able to confirm intratumoral replication of MV by recovery of replicating virus from the tumor as well as by in-situ hybridisation for MV N-specific mRNA. We were also able to confirm MV replication in tumors after intravenous injection of the virus by recovery of replicating virus and by RT-PCR for MV N-specific mRNA. No toxicity to the mice was observed, even after intravenous injection of 10<sup>7</sup> pfu of virus, although since the rodent is not naturally infectable by MV, toxic effects would be unlikely. Our data suggest that MV may have value as a replicating virus therapy for lymphomas. We are currently developing an immune competent, **measles** -virus infectable murine lymphoma model so that we can study this effect in the presence of pre-existing immunity to MV.

2000

84/3,AB/2 (Item 2 from file: 5)  
 DIALOG(R)File 5:BIOSIS Previews(R)  
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12482479 BIOSIS NO.: 200000235981

**Use of fusogenic membrane glycoproteins as novel therapeutic transgenes in gliomas.**

AUTHOR: **Russell S J** (a); Galanis Evanthia(a); Vile R(a); Johnson K(a);  
 James C D(a)  
 AUTHOR ADDRESS: (a)Mayo Clin, Rochester, NY\*\*USA  
 JOURNAL: Proceedings of the American Association for Cancer Research Annual  
 Meeting (41):p259 March, 2000  
 CONFERENCE/MEETING: 91st Annual Meeting of the American Association for  
 Cancer Research. San Francisco, California, USA April 01-05, 2000  
 ISSN: 0197-016X  
 RECORD TYPE: Citation  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 2000

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 DIALOG(R)File 357:Derwent Biotechnology Abs  
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0243877 DBA Accession No.: 1999-14642

**Use of fusogenic membrane glycoproteins as novel therapeutic transgenes in  
 gliomas- measles virus and gibbon-ape-leukemia virus glycoprotein  
 gene transfer by retro virus, adeno virus or plasmid vector for  
 potential glioma gene therapy (conference abstract)**

AUTHOR: Galanis E; Vile R; James C D; **Russell S J**  
 CORPORATE AFFILIATE: Mayo-Clin.Rochester  
 CORPORATE SOURCE: Mayo Clinic, Rochester, MN 55905, USA.  
 JOURNAL: Gene Ther. (6, Suppl.1, S7) 1999  
 ISSN: 0969-7128 CODEN: GETHEC  
 CONFERENCE PROCEEDINGS: Cytoreductive Gene Therapy Harold W. Siebens  
 Conference, Phillips Hall, Siebens Medical Education Building, Mayo  
 Foundation, Rochester, MN, USA, 25-27 September, 1999.  
 LANGUAGE: English

ABSTRACT: Virus fusogenic membrane glycoproteins from **measles** virus (MV),  
 MV glycoprotein-H and MV glycoprotein-F and a mutated form of the retro  
 virus envelope protein of gibbon-ape-leukemia virus (GALV.fus) were  
 used as therapeutic transgenes for **glioma** therapy. The U87 and U118  
**glioma** cell lines were stably transduced with the LacZ gene allowing  
 direct formation after staining with x-gal. The MV glycoprotein-F and  
 -H cDNAs were cloned into plasmid pCG vector and GALV.fus cDNA was  
 cloned into plasmid pCR3.1 vector. Co-transfection of the U87 and U118  
 cells with MV-F and MV-H lead in 48 hr to complete replacement of  
 monolayer culture by syncytia followed by massive cell death in 5-6  
 days. Transfection by MV-F or MV-H alone did not give cytopathic  
 effect. Cytotoxicity in the U87 and U118 cell lines was higher than the  
 cytotoxicity caused by transfection with herpes simplex virus  
 thymidine-kinase (EC-) gene followed by ganciclovir treatment. Similar  
 results were obtained with GALV.fus. The bystander effect in **glioma**  
 cell lines was high. Adeno virus and bicistronic retro viruses will be  
 produced. (0 ref)

**84/3,AB/4** (Item 2 from file: 357)  
 DIALOG(R)File 357:Derwent Biotechnology Abs  
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0243875 DBA Accession No.: 1999-14640

**Fusogenic membrane glycoproteins - a novel class of cytotoxic genes with  
 immunostimulatory properties- adeno virus and retro virus construction  
 for use in virus fusogenic membrane glycoprotein gene transfer for  
 tumor gene therapy and immunotherapy (conference abstract)**

AUTHOR: Bateman A; Murphy S; Emiliusen L; Ruchatz A; Melcher A;  
**Fielding A** ; Cattaneo R; Cosset F L; Russell S J; Vile R G  
 CORPORATE AFFILIATE: Mayo-Clin.Rochester

CORPORATE SOURCE: Molecular Medicine Program, Mayo Clinic, Rochester, MN 55905, USA.

JOURNAL: Gene Ther. (6, Suppl.1, S6) 1999

ISSN: 0969-7128 CODEN: GETHEC

CONFERENCE PROCEEDINGS: Cytoreductive Gene Therapy Harold W. Siebens Conference, Phillips Hall, Siebens Medical Education Building, Mayo Foundation, Rochester, MN, USA, 25-27 September, 1999.

LANGUAGE: English

ABSTRACT: Vius fusogenic membrane glycoproteins (FMGs) are a new class of therapeutic agents which have a direct cytotoxic effect through syncytia formation and stimulate effective antitumor immunity in vivo. FMG derived from morbili virus **measles** virus F and H glycoproteins, rhabdo virus vesicular-stomatitis virus-G glycoprotein, and retro virus envelope protein e.g. gibbon-ape-leukemia virus and mouse Moloney-leukemia virus were studied. Cytotoxic activity occurs by infected/transfected cells expressing FMG fusing with neighboring uninfected cells. The resultant syncytia evolve and eventually die via nonapoptotic mechanisms. When tested against a range of human tumor cells, FMGs had significantly higher cytotoxic activity in vitro than either herpes simplex virus thymidine-kinase/ganciclovir or CD-5FU. This is due to the FMG having a bystander effect at least a log higher than the suicide genes. Cytotoxicity is independent of the cell cycle. Retro virus and adeno viruses are being constructed for tumor gene therapy. Transplantable mouse tumor cell lines expressing FMG are effective vaccines against parental tumor challenge in vivo. Cytokines may be coexpressed with FMGs. (0 ref)

84/3,AB/5 (Item 3 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs

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0243871 DBA Accession No.: 1999-14636

**Redirecting measles virus hemagglutinin (H) protein to cancerous cells- surface display of carcinoembryonic antigen-specific single chain antibody on measles virus for use as gene therapy vector for cancer therapy (conference abstract)**

AUTHOR: Murphy A L; Zhang J; **Russell S J** ; Cattaneo R

CORPORATE AFFILIATE: Mayo-Clin.Rochester

CORPORATE SOURCE: Molecular Medicine Program, Mayo Clinic, Rochester, MN 55905, USA.

JOURNAL: Gene Ther. (6, Suppl.1, S4) 1999

ISSN: 0969-7128 CODEN: GETHEC

CONFERENCE PROCEEDINGS: Cytoreductive Gene Therapy Harold W. Siebens Conference, Phillips Hall, Siebens Medical Education Building, Mayo Foundation, Rochester, MN, USA, 25-27 September, 1999.

LANGUAGE: English

ABSTRACT: To attempt to retarget **measles** virus (MV) to **cancer** cells, a single chain antibody (scAb) specific for carcinoembryonic antigen (CAE) (a **cancer** -associated membrane glycoprotein) was displayed as a C-terminal fusion of the MV attachment protein, hemagglutinin (H). 3 Forms of the scAb were displayed with linker lengths of 0, 5, and 15 amino acids separating VH and VL domains. The H protein modified with the long linker scAb mediated cell-cell fusion preferentially in HeLa cells overexpressing CEA. The specificity of this interaction and its dependence on CEA was assessed. Most 0 and 5 amino acid linker scAb-H fusions lost the ability to mediate syncytium formation in HeLa and HeLa-CEA cells, possibly due to oligomerization causing steric hindrance. N-terminal display of these scAbs formed on a retro virus envelope protein showed that the short and zero linkers formed oligomers which inhibited virus-induced fusion. The longer linker scAb may act to positively redirect MV entry. This hybrid H protein is being built into a replication competent MV and further studies concerning

its ability to retarget the virus to CEA-expressing cells were presented. (0 ref)

84/3,AB/6 (Item 4 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs  
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0243869 DBA Accession No.: 1999-14634

**Replicating measles-based viruses with restricted cell tropism- measles virus vector for use in gene therapy (conference abstract)**

AUTHOR: Schneider U; Murphy A; Bulloagh F; Russell S J ; Cattaneo R

CORPORATE AFFILIATE: Mayo-Clin.Rochester

CORPORATE SOURCE: Molecular Medicine Program, Mayo Clinic, Rochester, MN 55905, USA.

JOURNAL: Gene Ther. (6, Suppl.1, S4) 1999

ISSN: 0969-7128 CODEN: GETHEC

CONFERENCE PROCEEDINGS: Cytoeductive Gene Therapy Harold W. Siebens Conference, Phillips Hall, Siebens Medical Education Building, Mayo Foundation, Rochester, MN, USA, 25-27 September, 1999.

LANGUAGE: English

ABSTRACT: The **measles** virus Edmonston strain is a nonsegmented negative strand RNA virus and is safe for human vaccination. By retargeting its cell entry it was transformed into a replicating vector for cytoeductive gene therapy. Towards this aim epidermal growth factor (EGF) or somatomedin-C (IGF) were displayed on the virus attachment protein hemagglutinin (H). Recombinant virus particles incorporating H/EGF or H/IGF in place of H were obtained. The H/EGF virus reached similar titers as standard **measles** virus on permissive cells, but only 100-500 times lower titers on cells expressing large amounts of the epidermal growth factor receptor. The infectivity of a virus with a Factor-Xa protease cleavage site between H and EGF was marginally increased by virus particle treatment with protease. Analysis of virus replication on different cells indicated tht the displayed EGF domain interfered with virus replication at the entry and other levels. A single chain antibody against carcinoembryonic antigen-1 was displayed on **measles** virus H. A hybrid protein maintained fusion-helper function in CEA-expressing cells. (0 ref)

84/3,AB/7 (Item 5 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs  
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0243868 DBA Accession No.: 1999-14633

**Regulated expression of fusogenic membrane glycoproteins- (conference abstract)**

AUTHOR: Linardakis E; Bateman A R; Murphy S M; Clackson T; Russell S ; Vile R G

CORPORATE AFFILIATE: Mayo-Clin.Rochester

CORPORATE SOURCE: Molecular Medicine Program, Guggenheim 18, Mayo Clinic, Rochester, MN 55905, USA.

JOURNAL: Gene Ther. (6, Suppl.1, S4) 1999

ISSN: 0969-7128 CODEN: GETHEC

CONFERENCE PROCEEDINGS: Cytoeductive Gene Therapy Harold W. Siebens Conference, Phillips Hall, Siebens Medical Education Building, Mayo Foundation, Rochester, MN, USA, 25-27 September, 1999.

LANGUAGE: English

ABSTRACT: Virus fusogenic membrane glycoproteins (FMG) are a new class of therapeutic genes that may be used to control tumor growth. FMG are virus envelope proteins that can bind to receptors on the target cells and cause the formation of multinucleated syncytia, composed of infected and uninfected fused cells, and eventually lead to cell death.

Some FMG (e.g. gibbon-ape-leukemia virus envelope and measles virus F1/H5) have been shown to have a dramatic cytotoxic effect against tumor cells in vitro (higher than herpes simplex virus thymidine-kinase (EC-2.7.1.21) suicide gene HSV tk/ganciclovir or CF/5FU, with a bystander effect at least a log higher). FMG kill tumor cells by mechanisms that are likely to be highly immunostimulatory. To control the cytotoxic effect of FMG, regulated expression systems were developed, where plasmid and virus vectors expressing FMGs from inducible promoters. Such systems would allow the production of delivery vehicles for in vivo and in vitro studies, and allow testing of the cytotoxic and immunostimulatory effects of FMG in defined in vitro systems and in in vivo systems. (0 ref)

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